UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,817	05/09/2001	Jochen Wolffgramm	MRI-1	4970

1473 7590 07/15/2003

FISH & NEAVE
1251 AVENUE OF THE AMERICAS
50TH FLOOR
NEW YORK, NY 10020-1105

EXAMINER	
JIANG, SHAOJIA A	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/851,817	WOLFFGRAMM, JOCHEN	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-10 and 12-25* is/are pending in the application.

4a) Of the above claim(s) *2-4,7-10,14-19 and 22-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6,12,13,20,21 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application is a continuation of PCT/EP99/08598 (International Filing Date: November 9, 1999 published in German and designated to US), which claims priority to EPO 98 12 1338.2. The certified copy of the priority documents have been received in the instant application. It is also noted that EPO 98 12 1338.2 is in German not in English.

Applicant's preliminary amendment in response to the Restriction Requirement in Paper No. 8, submitted May 2, 2003 in Paper No.10 is acknowledged, claim 25 is newly submitted.

Applicant's supplemental preliminary amendment submitted December 10, 2001 in Paper No.7(1/2) is acknowledged, wherein claim 11 is cancelled, and claims 4-5 and 7-8 have been amended, and claims 12-24 are newly submitted. Claim 1 has been cancelled in Applicant's preliminary amendment in Paper No. 5.

Currently, claims 2-10 and 12-25 are pending in this application.

Election/Restrictions

Applicant's election with traverse of the invention of Group II, claims 5-6, 12-21 and 25, and the invention of species (1) opioid dependency (2) a pharmaceutical composition comprising an opioid and prednisolone e.g., claim 25, submitted May 2, 2003 in Paper No.10 is acknowledged.

As discussed in the "Restriction Requirement" in the previous Office Action mailed November 22, 2002, inventions Group I and II are seen to be separate and distinct inventions since they are related as product and process of use. The criteria for distinct inventions: (1) the process for using the product as claimed can be practiced with another materially different product (MPEP § 806.05(h)). In the instant case, for example, a substitution treatment, e.g., administering methalone, may be used in the instant claimed method of treating opioid dependency herein.

It is noted that Albrecht et al. teaches that symptoms caused by each different addictive drug therein and drug withdraw and late sequences are different, i.e., symptoms caused by amphetamines, cnnabinoids, cocaine, and opioids, are different from each other (see entire article, particularly the 1st paragraph at page 1 of Albrecht et al., English translation, PTO-1449 submitted December 7, 2001). Albrecht et al. also teaches the different treatment for each different drug dependency or addiction therein. Thus, the teachings of Albrecht et al. support the examiner's position for the specie election for a single specific disease or condition to be treated since each different drug addictive condition to be treated is distinct from each other. The instant elected condition to be treated is opioid dependency.

Nonetheless, on consideration by the examiner, the specie election requirement for a single specific composition, particularly for a corticosteroid receptor agonist, is modified to include corticosteroid receptor agonists recited in claim 20 as a single specie in combination with an opioid, elected by Applicant in Paper No.10.

Therefore, the requirement is still deemed proper and is made FINAL.

Claims 2-4, 7-10 and 22-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 14-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected species.

The claims have been examined insofar as they read on the elected specie.

Claims 5-6, 12-13, 20-21 and 25 are examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-6 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for co-administering the particular corticosteroid receptor agonists recited in claim 20, and the particular addictive drugs disclosed in claims 13-19 and working examples in the specification (see page 22 of the specification herein) in composition to a host, does not reasonably provide enablement for co-administering any corticosteroid receptor agonists and any addictive drugs.

These recitations, "a corticosteroid receptor agonist" and "an addictive drug", are seen to be merely functional language.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a pharmaceutical composition for co-administering "a corticosteroid receptor agonist" and "an addictive drug".

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims 5-6 are deemed very broad since the broadest claim (i.e., claim 5) reads on any "corticosteroid receptor agonists" and "addictive drugs" employed in the composition herein.

The amount of direction or guidance presented:

Functional language at the point of novelty, as herein employed by Applicants, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997) at 1406: stating this usage does "little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". The

CAFC further clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphasis added).

In the instant case, "a corticosteroid receptor agonist" and "an addictive drug", recited in the instant claims are purely functional distinction. Hence, these functional recitations read on any compounds that might have the recited functions. However, the specification merely provides particular compounds for each kind of functional compounds for the composition (the elected invention).

Thus, Applicants functional language at the points of novelty fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph. Claims employing functional language at the exact point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al. supra*, at 468).

The predictability or unpredictability: the instant claimed invention is highly *unpredictable* as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully described genus, visualize or recognize the identity of the members of the genus, by structure, formula, or chemical name, of the claimed subject matter, as discussed above in *University of California v. Eli Lilly and Co.* Hence, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art is unable to fully predict possible physiological activities of any compounds having claimed functional properties in the pharmaceutical compositions herein.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects, side effects, and especially serious toxicity that may be generated by drug-drug interactions when and/or after administering to a host (e.g., a male) the ***combination*** of any compounds represented by "a corticosteroid receptor agonist" and "an addictive drug", which may encompass more than a thousand compounds. See text book "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9th ed, 1996) page 51 in particular. This book teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs

that are prescribed" and that "The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right column of page 51) (emphases added). In the instant case, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art is unable to fully predict possible adverse drug-drug interactions occurring with many combinations of any compounds having claimed functional properties in the pharmaceutical compositions herein to be administered to a host. Thus, the teachings of the book clearly support that the instant claimed invention is highly unpredictable.

The presence or absence of working examples and the quantity of experimentation necessary:

As discussed above, only particular compounds for each kind of functional compounds employed in the composition herein is disclosed in the specification, especially working examples at page 21-28. Thus, the specification fails to provide sufficient support of the broad use of any compounds having those functions recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of any compounds having those functions recited in the instant claims suitable to practice the claimed invention.

Further, as discussed above, Albrecht et al. teaches that symptoms caused by each different addictive drug herein and drug withdraw and late sequences are different, i.e., symptoms caused by amphetamines, cnnabinoids, cocaine, and opioids, are different from each other (see entire article, particularly the 1st paragraph at page 1 of

Albrecht et al., English translation, PTO-1449 submitted December 7, 2001). Albrecht et al. also teaches the different treatments of each different drug dependency or addiction herein. Thus, the teachings of Albrecht et al. support the examiner's position for lack of scope of enablement for the instant invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, the case *University of California v. Eli Lilly and Co.* (CAFC, 1997) and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims and their combinations employed in the claimed compositions to be administered to a host, with no assurance of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-6, 12-13, 20-21 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "a pharmacodynamic equivalent thereof" in claim 5 renders claim 5-6 indefinite. The expression "a pharmacodynamic equivalent thereof" is not seen to be clearly defined in the specification. Hence, one of ordinary skill in the art could not interpret the metes and bounds as to the recitation "a pharmacodynamic equivalent thereof" in the claim. Therefore, the scope of the claims is indefinite as to what would be considered "a pharmacodynamic equivalent thereof" encompassed thereby.

The recitations "a high dose" and "higher amount for the initial dosage" in claim 6 render claim 6 indefinite since these terms are relative terms. Hence, one of ordinary skill in the art could not interpret the metes and bounds as to these recitations in the claim. Therefore, the scope of the claims is indefinite as to what would be considered "a high dose" and "higher amount for the initial dosage" encompassed thereby.

The recitation "or" in claim 5 is improper language in a Markush group. Applicant is suggested to amend to use "and".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5, 12-13, 20-21 and 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Peyman (WO 9842275 as 102(b) prior art since it against the international filing date of 1999PCT/EP99/08598, PTO-892).

Peyman discloses the pharmaceutical composition comprising an opioid in combination with the instant preferred corticosteroid receptor agonist such as cortisol, cortisone, prednisolone, and dexamethasone (also known as a glucocrticoid) (see page 8 line 27 to page 9 line 1, and claims 1-2 and 15-17).

Thus, the disclosure of Peyman anticipates claim 5, 12-13, 20-21 and 25.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5-6, 12-13, 20-21 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Capasso et al. (XP-002100182 and XP-002100187, PTO-1449 submitted December 7, 2001) and Montgomery et al. (XP-002100181, PTO-1449 submitted December 7, 2001).

Capasso et al. discloses that a corticosteroid such as the instant preferred corticosteroid receptor agonist, dexamethasone, is capable of inhibiting opioid dependency and thus is useful in a pharmaceutical composition for the treatment of the opioid (opiate) dependency such as morphine by administering an effective amount of dexamethasone before or after the administration of morphine in its effective amount

(see two articles entirely, particularly abstract, XP-002100182 at page 743 and the right column of page 746 "Results", and XP-002100187).

Montgomery et al. also discloses that a corticosteroid such as the instant preferred corticosteroid receptor agonist, cortisol, is capable of reducing the severity of morphine withdrawal by administering an effective amount of dexamethasone in 2 mg/kg before or after the administration of morphine, i.e., administering a morphine pellet, 75 mg (see page 454 the left column).

Capasso et al. and Montgomery et al. do not expressly disclose a single composition comprising the particular additive drug in combination with the particular known corticosteroid receptor agonist. Capasso et al. and Montgomery et al. do not also expressly disclose the employment of the particular corticosteroid receptor agonist, prednisolone, in the treatment for the opioid (opiate) dependency.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the particular additive drug and a known corticosteroid receptor agonist in to a single composition.

One having ordinary skill in the art at the time the invention was made would have been motivated to combine an additive drug and the particular known corticosteroid receptor agonist such as a known corticosteroid, e.g., dexamethasone, cortisol, and prednisolone, in to a single composition since a corticosteroid is known to be useful in a composition and a method of treating the opioid (opiate) dependency based on the prior art. Therefore, one of ordinary skill in the art would have found it obvious to administer an additive drug and a corticosteroid receptor agonist together or

combine an additive drug and a corticosteroid receptor agonist such as a corticosteroid, e.g., dexamethasone, cortisol, and prednisolone, in to a single composition to be administered since a corticosteroid is known to inhibit or reduce opioid dependency.

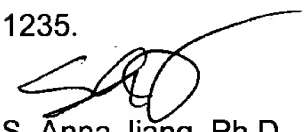
Thus the claimed invention as a whole is clearly prima facie obvious over the teachings of the prior art.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.



S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
June 27, 2003